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ORIGINAL ARTICLE

Predictors of referral for long-term EEG monitoring for Medicare beneficiaries with drug-resistant epilepsy

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Abstract

Objective: For people with drug-resistant epilepsy, the use of epilepsy surgery is low despite favorable odds of seizure freedom. To better understand surgery utilization, we explored factors associated with inpatient long-term EEG monitoring (LTM), the first step of the presurgical pathway.

Methods: Using 2001–2018 Medicare files, we identified patients with incident drug-resistant epilepsy using validated criteria of ≥2 distinct antiseizure medication (ASM) prescriptions and ≥1 drug-resistant epilepsy encounter among patients with ≥2 years pre- and ≥1 year post-diagnosis Medicare enrollment. We used multilevel logistic regression to evaluate associations between LTM and patient, provider, and geographic factors. We then analyzed neurologist-diagnosed patients to further evaluate provider/environmental characteristics.

Results: Of 12 044 patients with incident drug-resistant epilepsy diagnosis identified, 2% underwent surgery. Most (68%) were diagnosed by a neurologist. In total, 19% underwent LTM near/after drug-resistant epilepsy diagnosis; another 4% only underwent LTM much prior to diagnosis. Patient factors most strongly predicting LTM were age <65 (adjusted odds ratio 1.5 [95% confidence interval 1.3–1.8]), focal epilepsy (1.6 [1.4–1.9]), psychogenic non-epileptic spells diagnosis (1.6 [1.1–2.5]) prior hospitalization (1.7, [1.5–2]), and epilepsy center proximity (1.6 [1.3–1.9]). Additional predictors included female gender, Medicare/Medicaid non-dual eligibility, certain comorbidities, physician specialties, regional neurologist density, and prior LTM. Among neurologist-diagnosed patients, neurologist <10 years from graduation, near an epilepsy center, or epilepsy-specialized increased LTM likelihood (1.5 [1.3–1.9], 2.1 [1.8–2.5], 2.6 [2.1–3.1], respectively). In this model, 37% of variation in LTM completion near/after diagnosis was explained by individual neurologist practice and/or environment rather than measurable patient factors (intraclass correlation coefficient 0.37).

Significance: A small proportion of Medicare beneficiaries with drug-resistant epilepsy completed LTM, a proxy for epilepsy surgery referral. While some

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patient factors and access measures predicted LTM, non-patient factors explained a sizable proportion of variance in LTM completion. To increase surgery utilization, these data suggest initiatives targeting better support of neurologist referral.

KEYWORDS
epilepsy surgery, neurologist referral, presurgical evaluation, video EEG

1 | INTRODUCTION

There are about 1 000 000 people with drug-resistant epilepsy in the United States.[1] In addition to poorly controlled seizures, people with drug-resistant epilepsy suffer reduced quality of life, increased disability, substantial psychiatric comorbidities, and elevated risk of death.[2,3] Epilepsy surgery with resection offers a 30%–70% cure rate,[4–6] as compared to a <5% chance of seizure freedom with continued trials of antiseizure medication (ASM).[7,8] Yet it is believed that epilepsy surgery rates are persistently low since the landmark 2001 randomized controlled trial that first established the efficacy of anterior temporal lobectomy resective surgery.[9–11]

While there are undoubtedly multiple barriers to undergoing epilepsy surgery,[12] research has shown that one of the primary drivers is inadequate referral for presurgical evaluation.[13–19] This is the initial step, in which a person's physician refers him or her for inpatient long-term EEG monitoring (LTM) to better characterize the seizures and to determine surgical candidacy. Prior literature demonstrates that the majority of people with active epilepsy are seen by neurologists,[20–22] and thus neurologists are critical gatekeepers to treatment escalation. Improving provider, and in particular neurologist, referral is paramount to increasing utilization of epilepsy surgery.

In this study, we sought to better understand patient, provider, and geographic factors associated with completion of LTM among Medicare beneficiaries. While LTM may be an imperfect proxy for epilepsy surgery referral, this approach should characterize the upper bound of those referred for epilepsy surgery. The goal of this work is to identify opportunities to improve patient access to evaluation for the most effective therapy for drug-resistant epilepsy—epilepsy surgery—and to inform possible interventions directed at neurology providers.

Key points

- Despite strong efficacy, epilepsy surgery rates remain low.
- Referral for inpatient long-term EEG monitoring (LTM) is the typical first step of the presurgical evaluation pathway.
- Only 19% of Medicare beneficiaries with incident drug-resistant epilepsy underwent LTM near (within 60 days) or after diagnosis and only 2% underwent surgery.
- Several patient factors and measures of access to care predicted LTM completion.
- A large proportion of variation in referral for LTM was explained by a neurologist's practice or environmental factors.

2 | METHODS

2.1 | Datasets

We used a 20% sample of fee-for-service Medicare Carrier Files from 2001 to 2018. While this dataset largely captures individuals over 65 years, Medicare also includes many younger patients with drug-resistant epilepsy who are disabled.[23] Additionally, Medicare provides national data, large sample size, and allows considerations of neurologist characteristics and geographic density. We included Medicare beneficiaries continuously enrolled in Parts A, B, and D. Additionally, we linked provider data from the American Medical Association (AMA) Physician Masterfile, and we identified epilepsy centers and locations using the National Association of Epilepsy Centers (NAEC) accreditation statuses.[24]

2.2 | Population

We identified patients with drug-resistant epilepsy using the validated criteria of (1) ≥1 encounter (clinic, consultation, inpatient, or emergency department [ED] visit) with a drug-resistant or intractable epilepsy ICD diagnosis code, and (2) ≥2 distinct ASM claims. Our prior work validated this administrative claims-based definition of drug-resistant epilepsy, which has a sensitivity of 86% and a specificity 74%.[25] Of note, in our previous validation work, we assessed the performance of a range of definitions,

including a more specific definition that only counted nongabapentinoid ASMs, but for this current study we chose the definition with the best predictiveness overall.[25]

In this study, we next applied exclusion criteria to allow a two-year "washout" period prior to the patient's first captured drug-resistant epilepsy diagnosis encounter (index encounter) to sample a cohort with newly diagnosed drug-resistant epilepsy. To support a sufficient washout period, the following exclusion criteria were applied: an index encounter before 2010 (while diagnoses were available for review from 2001 forward, drug information was only available from 2008 onward), <2 years of continuous Part A/B/D coverage before the index encounter, non-encounter-associated drug-resistant epilepsy diagnosis codes in the 2 years prior to the index encounter (to identify new diagnoses, but allowing an exception for codes generated 60 days prior to the index encounter as pre-visit testing), and any epilepsy surgery (diagnostic or therapeutic) prior to the index encounter. Additionally, we applied exclusion criteria to support sufficient follow-up to assess study outcomes: an index encounter after 2017 and <1 year of continuous Part A/B/D coverage after index encounter. Lastly, we excluded patients age <18 years and with residence outside the United States.

2.3 | Outcomes and predictor variables

The primary outcome was completion of LTM, previously used as a proxy for epilepsy surgery referral,[13,14] which was identified by both (1) an ICD or CPT code for LTM (ICD-9 89.19; ICD-10 4A10X4Z; CPT 95951, 95956) and (2) an admitting or principal epilepsy diagnosis code (ICD-9 345.x, 780.3x; ICD-10 G40.x, R56.x). This definition was based on previously applied claims definitions for LTM[14,26,27] as well as a recently validated claims definition for epilepsy monitoring unit (EMU) admissions.[28] The primary outcome had to occur near (within 60 days, to accommodate pre-visit testing) or after index encounter. Only elective admissions were included in the primary outcome to exclude urgent LTM (e.g., those for status epilepticus). We also measured the outcome of epilepsy surgery including resection, ablation, and neurostimulation with vagus nerve stimulation (VNS), responsive neurostimulation (RNS), or deep brain stimulation (DBS). While resection or ablation are typically undertaken with a goal of seizure freedom and neurostimulation is typically undertaken as a palliative procedure, we were interested in capturing all therapeutic procedures as referral for epilepsy surgery evaluation is upstream of all surgical procedures.

Criteria for definitions of each outcome and covariate are presented in Table S1. The predictor variables evaluated included age (dichotomized as <65 or ≥65 years, as older age may influence provider consideration of surgery[15]), sex, race (white, Black, Hispanic, other, or missing), Medicare/Medicaid dual eligibility, year of index encounter, epilepsy type by diagnosis code (generalized, focal, or unknown), indicators of disease severity over the prior 2 years (i.e., 3+ ASMs, any hospitalizations for epilepsy, any ED visits for epilepsy), neurologic comorbidities (traumatic brain injury, headache, stroke, dementia, brain tumor, intellectual disability/developmental delay), psychiatric comorbidities (anxiety, depression, bipolar disorder, alcohol/substance abuse, psychogenic non-epileptic spells [PNES]), Charlson comorbidity score (categorized as 0, 1, 2, 3+; excluding dementia and stroke as these were previously accounted for), diagnosing provider type (primary care physician [PCP], neurologist, neurosurgeon, emergency medicine [EM] physician, nurse practitioner[NP]/physician assistant[PA], or other), hospital referral region (HRR) neurologist density quintile (1st quintile lowest, 5th quintile highest),[29] prior LTM 60+ days before diagnosis (included as a notable proportion of patients underwent LTM to clarify their diagnosis prior to receiving a diagnosis of drug-resistant epilepsy), and distance to the nearest epilepsy center (dichotomized as <50 miles or ≥50 miles).

In a secondary analysis to further evaluate the role of provider characteristics, we considered only patients who had their index encounter with a neurologist. We first identified the cohort of neurologists with ≥25 evaluation and management (E/M) Medicare claims in total from 2010 to 2018 as a threshold for meaningful clinical practice during the study period. Then, we sought to identify epilepsy specialists, which are not specifically identified in the Medicare provider taxonomy. Among neurologists with at least 25 E/M claims, the 90th percentile had 20% of their claims during the study period associated with an epilepsy diagnosis; thus, these neurologists and those with a higher proportion of epilepsy visits were considered epilepsy specialists. This cutoff is consistent with a recent American Academy of Neurology (AAN) member survey in which 10% of responding neurologists indicated they specialized in epilepsy.[30] Using the AMA Physician Masterfile, we queried additional physician characteristics for the neurologist cohort identified in our Medicare dataset: graduation year (<10 years prior or ≥10 years prior to start of study period), sex, primary specialty, practice address in the same ZIP code as an epilepsy center, and census region. Lastly, as additional subgroup analyses, we looked for differences in predictors for patients under 65 years and for patients with a focal epilepsy diagnosis.

2.4 | Statistical analysis

Patient characteristics, provider characteristics, and geographic factors are reported as categorical frequencies and/or mean with the appropriate respective tests applied for significance in the comparison of those who underwent LTM to those who did not. We used a generalized linear mixed model (Proc Glimmix with a log link) to evaluate the association between our primary outcome (LTM) and pre-specified factors of patient characteristics (age, sex, race, dual eligibility, index encounter year, epilepsy type, ASMs, hospitalizations/ED visits for epilepsy in the last two years, and comorbidities), diagnosing provider type, and geography/access (neurologist density, prior LTM, and proximity to an accredited comprehensive epilepsy center) with a random intercept for diagnosing physicians to account for the correlation of treatment patterns within a particular diagnosing physician's patient group. In our second model that was limited to neurologists' patients, we included additional provider characteristics (graduation year, sex, specialty information, provider proximity to an epilepsy center, and census region) in the generalized linear mixed model clustering by neurologists to assess the relationship between provider characteristics and LTM usage. Because LTM is a proxy for epilepsy surgery referral, we also conducted sensitivity analyses for both models using a primary composite outcome of LTM or epilepsy surgery (to make sure we captured all patients who underwent epilepsy surgery including VNS implantation which may not necessitate LTM). All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

3 | RESULTS

3.1 | Study population demographics

We identified 12044 patients with an incident drug-resistant epilepsy diagnosis (Figure 1). The mean age was 58 years (standard deviation 17) with 60% under 65 years of age. Of this population, 55% were female, 73% were white, and 16% were Black. The most common neurologic comorbidities identified were stroke (22%), intellectual disability/developmental delay (18%), and headache (18%). The most common psychiatric comorbidities were anxiety (23%), depression (16%), and alcohol/substance abuse (16%). Nearly half (45%) had focal epilepsy diagnoses while 23% had generalized epilepsy diagnoses at their incident drug-resistant epilepsy encounter. Most patients (68%) were seen by a neurologist at their index encounter (i.e., first encounter for drug-resistant epilepsy) and 71% lived <50 miles from an epilepsy center. A comprehensive list of demographic characteristics and significant differences stratified by outcome are presented in Table 1.

3.2 | Pathways of care

Patients progressed through their care differently, though there were a limited number of possible pathways, and the vast majority never underwent LTM (77%) within the study period. In total, 19% (2301/12044) underwent LTM near (within 60 days) or after their index encounter; of these patients, 11% (256/2301) underwent LTM both before (60+ days prior) and near or after their index encounter. The median time from index encounter to LTM was 29 days (interquartile range 1–390 days). An additional 4% (431/12044) underwent LTM only 60+ days prior to their index encounter. Only 2% (294/12044) of patients with drug-resistant epilepsy underwent any therapeutic epilepsy surgery during the study period (including resection procedures [34], ablation [1], and neurostimulation [267]; some patients had multiple procedures). About half (157/294) of these patients had epilepsy surgery without LTM near or after diagnosis. Of these 157 patients without an observed LTM claim, three underwent resection procedures and 154 had neurostimulation (three had procedure codes specific to RNS/DBS and 151 had procedure codes specific to VNS or were presumed to have VNS based on neurostimulation codes). We compared the population of patients who underwent VNS without LTM near or at diagnosis ($N=151$) to the population that underwent LTM and completed surgery ($N=137$); we found those who went straight to VNS typically had less severe disease (as measured by hospitalizations and ER visits) and less access to epilepsy care (as measured by neurologist density, prior LTM completion, and proximity to an epilepsy center).

3.3 | Predictors of LTM

Multiple predictors were associated with LTM in the generalized linear mixed model (see Table 1). Patient factors associated with LTM completion included age <65 (adjusted odds ratio 1.5 [95% confidence interval 1.3–1.8]), female sex (1.2 [1.02–1.3]), and those not dual-eligible for Medicare and Medicaid (1.4 [1.2–1.7]). Patients with a focal drug-resistant epilepsy diagnosis were more likely to complete LTM as compared to patients with drug-resistant generalized epilepsy (1.6 [1.4–1.9]). Markers of disease severity were associated with increased likelihood of LTM including 3+ ASMs (1.4 [1.2–1.6]), prior epilepsy hospitalizations (1.7 [1.5–2.0]), and prior epilepsy ED visit

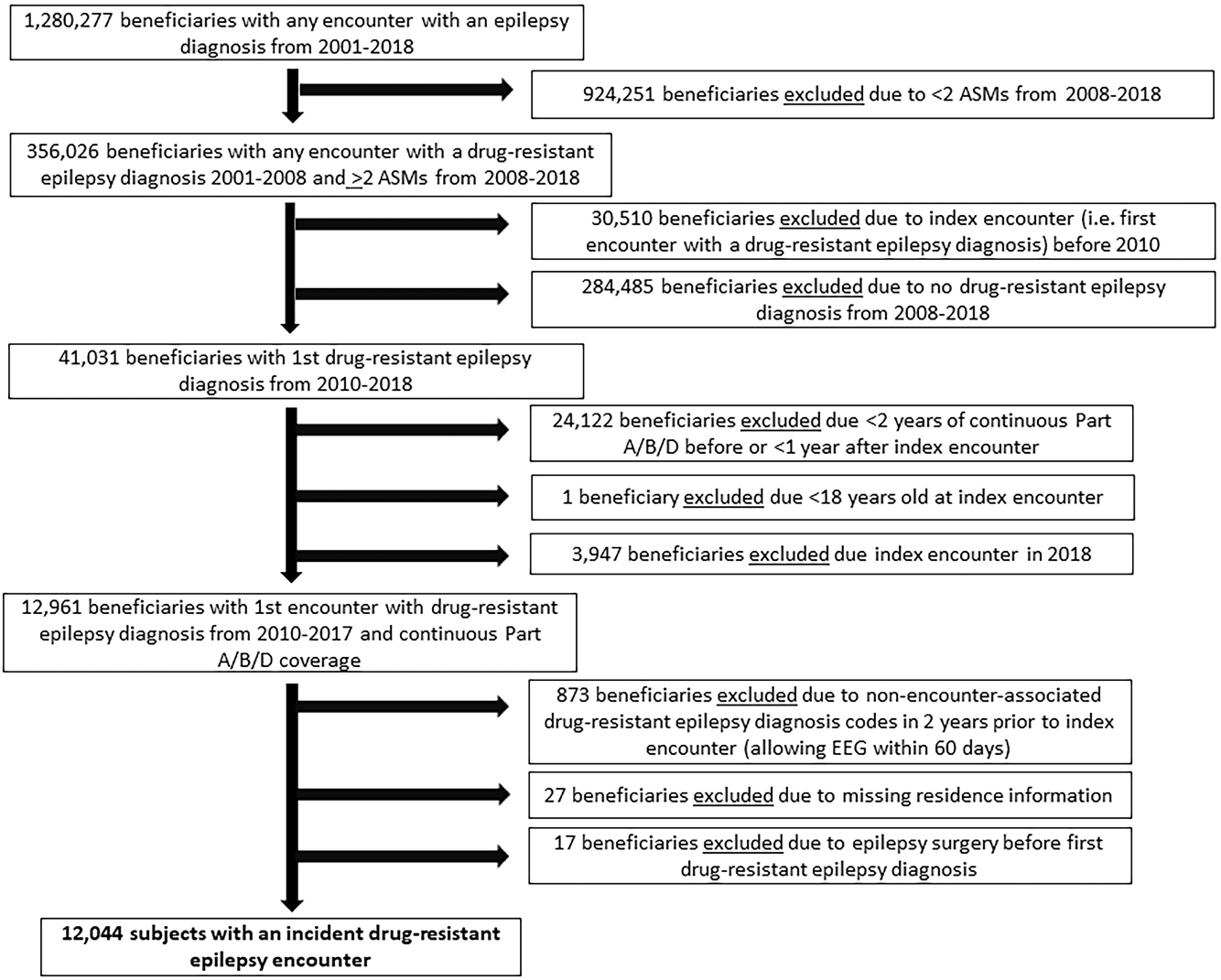

FIGURE 1 Study population diagram.

(1.4 [1.3–1.7]). Comorbidities of traumatic brain injury (1.5 [1.1–1.9]), headache (1.3 [1.1–1.5]), dementia (1.2 [1.01–1.4]), and PNES (1.6 [1.1–2.5]) were also associated with LTM.

Certain diagnosing physician specialties increased the likelihood of LTM as compared to primary care (neurology 1.9 [1.6–2.3], neurosurgery 2.1 [1.1–3.7], emergency medicine 1.8 [1.3–2.4]). Additionally, residing in high neurologist density regions (5th quintile 1.6 [1.3–2.1]; reference 1st quintile) and residing <50 miles from an epilepsy center (1.6 [1.3–1.9]) were associated with LTM. Lastly, LTM completion 60+ days prior to drug-resistant epilepsy diagnosis was associated with increased likelihood of LTM near or after diagnosis (1.8 [1.5–2.3]). For this model, the c statistic was 0.94, and the intraclass correlation coefficient was 0.42, or said differently, 42% of variation in LTM completion near or after diagnosis was explained by the individual provider's practice and/or provider's environment.

3.4 | Subanalysis of predictors of LTM for patients diagnosed by neurologists

We identified 15 564 neurologists who had ≥25 E/M Medicare claims in the study period from 2008 to 2018. Of these neurologists, 7454 (48%) had any services linked to a drug-resistant epilepsy diagnosis; on average, 2% of neurologist services were linked to a drug-resistant epilepsy diagnosis. Among the 14 704 neurologists who could be linked to AMA Physician Masterfile data, 10 077 (69%) graduated 10+ years before the study period began and 4352 (30%) were female. The practice address was in a ZIP code that contained an epilepsy center for 6533 (44%).

Of the total 15 564 neurologists, we identified 1741 neurologists as epilepsy specialists. For epilepsy specialists, an average 11% of services were linked to a drug-resistant epilepsy diagnosis. Among the 1640 epilepsy specialists who could be linked to AMA Physician Masterfile data, the majority (66%) graduated 10+ years before the study

TABLE 1 Patients of all providers: Characteristics and predictors of inpatient LTM EEG.

(Continues)

	Total *N* (%) 12 044	LTM near/after diagnosis *N* (%) 2301 (19.1)	No LTM near/after diagnosis *N* (%) 9743 (80.9)	*p* value	LTM multivariable OR (95% CI) *N* = 11 907[a] *c* statistic = 0.94	*p* value
Age, mean (SD)	58 (17)	56 (17)	59 (17)	<0.01		
<65	7202 (59.8)	1466 (63.7)	5736 (58.9)	<0.01	1.5 (1.3–1.8)	<0.01
65+	4842 (40.2)	835 (36.3)	4007 (41.1)		Reference	
Sex				<0.01		
Female	6612 (54.9)	1337 (58.1)	5275 (54.1)		1.2 (1.02–1.3)	0.02
Race				0.35		
White	8765 (72.8)	1680 (73)	7085 (72.7)		Reference	
Black	1961 (16.3)	391 (17)	1570 (16.1)		1.1 (0.9–1.3)	0.48
Hispanic	920 (7.6)	159 (6.9)	761 (7.8)		0.9 (0.7–1.2)	0.49
Others/missing	398 (3.3)	71 (3.1)	327 (3.4)		0.9 (0.7–1.3)	0.57
Dual eligibility						
Yes	8566 (71.1)	1589 (69.1)	6977 (71.6)	0.02	Reference	
No	3478 (28.9)	712 (30.9)	2766 (28.4)		1.4 (1.2–1.7)	<0.01
Diagnosis year				0.06		
2010	1415 (11.8)	240 (10.4)	1175 (12.1)		Reference	
2011	1503 (12.5)	316 (13.7)	1187 (12.2)		1.2 (0.9–1.5)	0.14
2012	1387 (11.5)	250 (10.9)	1137 (11.7)		1.0 (0.8–1.3)	0.94
2013	1374 (11.4)	271 (11.8)	1103 (11.3)		1.2 (0.9–1.5)	0.2
2014	1353 (11.2)	264 (11.5)	1089 (11.2)		1.1 (0.8–1.4)	0.64
2015	1724 (14.3)	355 (15.4)	1369 (14.1)		1.2 (1–1.5)	0.13
2016	1712 (14.2)	305 (13.3)	1407 (14.4)		1 (0.8–1.2)	0.7
2017	1576 (13.1)	300 (13)	1276 (13.1)		1.1 (0.8–1.4)	0.6
Epilepsy type				<0.01		
Focal	5444 (45.3)	1219 (53)	4225 (43.4)		1.6 (1.4–1.9)	<0.01
Generalized	2732 (22.7)	414 (18)	2318 (23.8)		Reference	
Unknown	3868 (32.1)	668 (29)	3200 (32.8)		1.2 (1–1.4)	0.07
Disease severity (in prior 2 years)						
3+ ASMs	3142 (26.1)	751 (32.6)	2391 (24.5)	<0.01	1.4 (1.2–1.6)	<0.01
Prior hospitalizations	2151 (17.9)	582 (25.3)	1569 (16.1)	<0.01	1.7 (1.5–2)	<0.01
Prior ED visit	3193 (26.5)	747 (32.5)	2446 (25.1)	<0.01	1.4 (1.3–1.7)	<0.01
Neurologic comorbidities						
TBI	519 (4.3)	135 (5.9)	384 (3.9)	<0.01	1.5 (1.1–1.9)	<0.01
Headache	2123 (17.6)	534 (23.2)	1589 (16.3)	<0.01	1.3 (1.1–1.5)	<0.01
Stroke	2658 (22.1)	557 (24.2)	2101 (21.6)	<0.01	1.2 (1–1.4)	0.04
Dementia	1789 (14.9)	314 (13.7)	1475 (15.1)	0.07	0.9 (0.7–1)	0.08
Brain tumor	537 (4.5)	133 (5.8)	404 (4.2)	<0.01	1.2 (0.9–1.6)	0.14
Intellectual disability/ developmental delay	2175 (18.1)	418 (18.2)	1757 (18)	0.88	1.04 (0.9–1.2)	0.66
Psychiatric comorbidities						
Anxiety	2764 (22.9)	619 (26.9)	2143 (22)	<0.01	1.2 (1–1.3)	0.07
Depression	1914 (15.9)	411 (17.9)	1503 (15.4)	<0.01	1.1 (0.9–1.3)	0.55
Bipolar disorder	1215 (10.1)	248 (10.8)	967 (9.9)	0.22	0.9 (0.7–1.1)	0.23
Alcohol/substance abuse	1910 (15.9)	426 (18.5)	1484 (15.2)	<0.01	1.1 (1–1.4)	0.12
PNES	203 (1.7)	70 (3)	133 (1.4)	<0.01	1.6 (1.1–2.5)	0.02

TABLE 1 (Continued)

	Total *N* (%) 12044	LTM near/after diagnosis *N* (%) 2301 (19.1)	No LTM near/after diagnosis *N* (%) 9743 (80.9)	*p* value	LTM multivariable OR (95% CI) *N* = 11907[a] *c* statistic = 0.94	*p* value
Charlson score (excluding dementia, stroke)				0.03		
0	4662 (38.7)	837 (36.4)	3825 (39.3)		Reference	
1	2160 (17.9)	451 (19.6)	1709 (17.5)		1.2 (1–1.4)	0.06
2	1700 (14.1)	328 (14.3)	1372 (14.1)		1 (0.9–1.3)	0.67
3+	3522 (29.2)	685 (29.8)	2837 (29.1)		1.1 (0.9–1.2)	0.58
Diagnosing physician				<0.01		
Neurologist	8137 (67.6)	1635 (71.1)	6502 (66.7)		1.9 (1.6–2.3)	<0.01
Neurosurgeon	126 (1.1)	31 (1.4)	95 (1)		2.1 (1.1–3.7)	0.02
EM	694 (5.8)	142 (6.2)	552 (5.7)		1.8 (1.3–2.4)	<0.01
PCP	1881 (15.6)	232 (10.1)	1649 (16.9)		Reference	
NP or PA	456 (3.8)	68 (3)	388 (4)		1.4 (0.9–2.0)	0.1
Other/unknown[a]	750 (6.2)	193 (8.4)	557 (5.7)		1.6 (1.2–2.2)	<0.01
Neurologist density quintile				<0.01		
1st quintile (low)	1260 (10.5)	182 (7.9)	1273 (13.1)		Reference	
2nd quintile	1664 (13.8)	252 (11)	1802 (18.5)		1 (0.7–1.3)	0.83
3rd quintile	2044 (17)	302 (13.1)	1947 (20)		0.8 (0.6–1.1)	0.19
4th quintile	3232 (26.8)	609 (26.5)	2530 (26)		1 (0.8–1.4)	0.74
5th quintile (high)	3844 (31.9)	956 (41.6)	2191 (22.5)		1.6 (1.3–2.1)	<0.01
Prior LTM EEG	687 (5.7)	256 (11.1)	431 (4.4)	<0.01	1.8 (1.5–2.3)	<0.01
Distance to nearest epilepsy center						
Mean (SD)	41.7 (72.2)	30.9 (50)	44 (76)	<0.01		
<50 miles	8583 (71.3)	1852 (80.5)	6731 (69.1)		1.6 (1.3–1.9)	<0.01
50+ miles	3461 (28.7)	449 (19.5)	3012 (30.9)	<0.01	Reference	

[a]Excludes 137 patients with unknown diagnosing physician information.

period began and 31% were female. (Of note, of those neurologists who graduated <10 years before the study period began, 49% were female). The practice address was in a ZIP code that contained an epilepsy center for 58%. Epilepsy specialists were fairly evenly distributed across census regions.

There were 7913 patients diagnosed by a neurologist, 5555 (70%) were diagnosed by a non-epilepsy specialist neurologist, and 2358 (30%) were seen by an epilepsy specialist. Demographics and predictors of LTM for these subsets of patients first seen for drug-resistant epilepsy by neurologists linkable to the AMA Physician Masterfile are reported in Table 2. In general, significant patient factor predictors are similar as those significant for the full patient cohort seen by all provider types. Particularly notable are several of the provider characteristics. Being seen by a neurologist <10 years out from graduation was associated with an increased likelihood of LTM (adjusted odds ratio 1.5 [95% confidence interval 1.3–1.9]). Being seen by a neurologist in the census regions of Midwest, South, and West was associated with a lower likelihood of LTM as compared to the Northeast (0.7 [0.6–0.95], 0.8 [0.6–0.95], 0.6 [0.5–0.8], respectively). Neurologists near an epilepsy center (defined as an epilepsy center within the provider's ZIP code) were associated with increased likelihood of LTM (2.1 [1.8–2.5]). Epilepsy specialists were also associated with increased likelihood of LTM (2.6 [2.1–3.1]). For this model predicting LTM among neurologist-diagnosed patients, the c statistic was 0.89 and the intraclass correlation coefficient was 0.37 (37% of variation in LTM completion near or after diagnosis was explained by the individual neurologist's practice and/or provider's environment.)

3.5 | Sensitivity analyses

Because LTM is a *proxy* for epilepsy surgery referral, we repeated the primary and subset analyses using a primary composite outcome of LTM or epilepsy surgery (to make sure we captured all patients who underwent epilepsy

TABLE 2 Patients of neurologists: Patient and provider characteristics and predictors of inpatient LTM EEG.

	Neurologist (non-epilepsy specialist) patients *N* (%) 5555 (70.2)	Epilepsy specialist patients *N* (%) 2358 (29.8)	*p* value	LTM multivariable OR (95% CI) *N* = 7927 *c* statistic = 0.89	*p* value
Age, mean (SD)	60 (17)	55 (17)	<0.01		
<65	3091 (55.6)	1614 (68.5)	<0.01	1.4 (1.1–1.6)	<0.01
65+	2464 (44.4)	744 (31.6)		Reference	
Sex			0.49		
Female	3083 (55.5)	1289 (54.7)		1.2 (1.02–1.4)	0.02
Race			0.41		
White	4129 (74.3)	1756 (74.5)		Reference	
Black	819 (14.7)	358 (15.2)		1 (0.8–1.2)	0.8
Hispanic	414 (7.5)	179 (7.6)		0.8 (0.6–1)	0.1
Others/missing	193 (3.5)	65 (2.8)		0.9 (0.6–1.3)	0.63
Dual eligibility					
Yes	3788 (68.2)	1727 (73.2)	<0.01	Reference	
No	1767 (31.8)	631 (26.8)		1.3 (1.1–1.6)	<0.01
Diagnosis year			0.02		
2010	681 (12.3)	333 (14.1)		Reference	
2011	611 (11)	305 (12.9)		1.3 (1–1.7)	0.05
2012	667 (12)	283 (12)		1.1 (0.8–1.4)	0.63
2013	668 (12)	259 (11)		1.3 (1–1.7)	0.09
2014	681 (12.3)	255 (10.8)		1.3 (1–1.7)	0.09
2015	821 (14.8)	332 (14.1)		1.2 (1–1.6)	0.11
2016	741 (13.3)	327 (13.8)		1 (0.8–1.3)	0.96
2017	685 (12.3)	264 (11.2)		1.2 (0.9–1.6)	0.21
Epilepsy type			<0.01		
Focal	2851 (51.3)	1560 (66.2)		1.3 (1.1–1.5)	0.02
Generalized	1444 (26)	373 (15.8)		Reference	
Unknown	1260 (22.7)	425 (18)		1.2 (0.9–1.5)	0.15
Disease severity (in prior 2 years)					
3+ ASMs	1376 (24.8)	703 (29.8)	<0.01	1.4 (1.2–1.6)	<0.01
Prior hospitalizations	983 (17.7)	355 (15.1)	<0.01	1.8 (1.5–2.1)	<0.01
Prior ED visit	1313 (23.6)	630 (26.7)	<0.01	1.4 (1.2–1.6)	<0.01
Neurologic comorbidities					
TBI	237 (4.3)	81 (3.4)	0.09	1.3 (1–1.9)	0.08
Headache	985 (17.7)	394 (16.7)	0.27	1.4 (1.2–1.7)	<0.01
Stroke	1310 (23.6)	368 (15.6)	<0.01	1.1 (0.9–1.3)	0.28
Dementia	829 (14.9)	225 (9.5)	<0.01	0.8 (0.7–1)	0.09
Brain tumor	255 (4.6)	101 (4.3)	0.55	1.4 (1–1.9)	0.04
Intellectual disability/ developmental delay	855 (15.4)	483 (20.5)	<0.01	1 (0.8–1.2)	0.93
Psychiatric comorbidities					
Anxiety	1246 (22.4)	485 (20.6)	0.07	1.1 (1–1.4)	0.13
Depression	876 (15.8)	336 (14.3)	0.09	1.1 (0.9–1.3)	0.51

(Continues)

TABLE 2 (Continued)

	Neurologist (non-epilepsy specialist) patients *N* (%) 5555 (70.2)	Epilepsy specialist patients *N* (%) 2358 (29.8)	*p* value	LTM multivariable OR (95% CI) *N* = 7927 *c* statistic = 0.89	*p* value
Bipolar disorder	516 (9.3)	227 (9.6)	0.64	0.9 (0.7–1.1)	0.35
Alcohol/substance abuse	840 (15.1)	322 (13.7)	0.09	1.7 (1.1–1.3)	0.4
PNES	75 (1.4)	39 (1.7)	0.3	1.7 (1.1–2.8)	0.03
Charlson score (excluding dementia, stroke)			<0.01		
0	2091 (37.6)	1113 (47.2)		Reference	
1	1015 (18.3)	440 (18.7)		1.2 (1–1.4)	0.14
2	794 (14.3)	287 (12.2)		1.1 (0.9–1.4)	0.44
3+	1655 (29.8)	518 (22)		1.1 (0.9–1.3)	0.59
Neurologist density quintile			<0.01		
1st quintile (low)	617 (11.1)	217 (9.2)		Reference	
2nd quintile	791 (14.2)	253 (10.7)		0.9 (0.6–1.2)	0.35
3rd quintile	966 (17.4)	383 (16.2)		0.9 (0.7–1.2)	0.47
4th quintile	1514 (27.3)	648 (27.5)		0.9 (0.7–1.2)	0.44
5th quintile (high)	1667 (30)	857 (36.3)		1.3 (1–1.7)	0.1
Prior LTM EEG	247 (4.5)	211 (9)	<0.01	1.5 (1.2–1.9)	<0.01
Distance to nearest epilepsy center					
Mean (SD)	44.7 (79.1)	33.7 (41.6)	<0.01		
<50 miles	3860 (69.5)	1771 (75)	<0.01	1.2 (1–1.5)	0.03
50+ miles	1695 (30.5)	587 (25)		Reference	
Provider sex			<0.01		
Female	1275 (23)	645 (27.4)		1 (0.8–1.2)	0.68
Provider graduation date <10 years	938 (16.9)	430 (18.2)	0.15	1.5 (1.3–1.9)	<0.01
Provider census region			<0.01		
Northeast	927 (16.7)	529 (22.4)		Reference	
Midwest	1318 (23.7)	567 (24.1)		0.7 (0.6–0.9)	<0.01
South	2475 (44.6)	891 (37.8)		0.8 (0.6–0.95)	<0.01
West	832 (15)	371 (15.7)		0.6 (0.5–0.8)	<0.01
Outside of US/unknown	3 (0.1)	0 (0)		1.8 (0.1–34.7)	0.80
Epilepsy specialist provider	0 (0)	2358 (100)	–	2.6 (2.1–3.1)	<0.01
Provider in epilepsy center ZIP	1260 (22.7)	1322 (56.1)	<0.01	2.1 (1.8–2.5)	<0.01

surgery including VNS implant which may not necessitate LTM). We found patient characteristics and provider characteristic predictors to be similar for the combined outcome for both the model of all patients and the model of patients of neurologists. These results are presented in Table 3. We repeated analyses for only patients under 65 years of age; as may be expected, there was a slightly higher proportion of patients who underwent LTM (20%) and surgery (3.8%), but predictors were similar to the primary analysis. We also repeat analyses for only patients with a focal epilepsy diagnosis, and again found a higher rate of LTM (22%) and surgery (3.1%), with predictors similar to the primary analysis.

4 | DISCUSSION

We found that for Medicare beneficiaries with incident drug-resistant epilepsy, patient factors strongly associated with LTM completion included younger age, focal epilepsy,

TABLE 3 Predictors of composite outcome LTM EEG or epilepsy surgery.

	Full cohort model: Patients of all providers		Subanalysis model: Patients of neurologists	
	LTM or surgery multivariable OR (95% CI) $N = 11\,907$ c statistic = 0.93	p value	LTM or surgery multivariable OR (95% CI) $N = 7913$ c statistic = 0.88	p value
Age				
<65	1.6 (1.4–1.9)	<0.01	1.4 (1.2–1.7)	<0.01
65+	Reference		Reference	
Sex				
Female	1.2 (1.04–1.3)	<0.01	1.2 (1.04–1.4)	0.01
Race				
White	Reference		Reference	
Black	1 (0.9–1.2)	0.82	0.9 (0.8–1.2)	0.54
Hispanic	0.9 (0.7–1.1)	0.17	0.7 (0.6–0.98)	0.03
Others/missing	0.9 (0.7–1.2)	0.49	0.9 (0.6–1.5)	0.51
Dual eligibility				
Yes	Reference		Reference	
No	1.4 (1.2–1.6)	<0.01	1.3 (1.1–1.5)	<0.01
Diagnosis year				
2010	Reference		Reference	
2011	1.2 (0.9–1.5)	0.17	1.3 (1–1.7)	0.05
2012	1 (0.8–1.2)	0.8	1 (0.8–1.3)	0.98
2013	1.2 (0.9–1.5)	0.2	1.3 (1–1.7)	0.09
2014	1.1 (0.8–1.3)	0.7	1.2 (0.9–1.6)	0.14
2015	1.1 (0.9–1.4)	0.24	1.2 (0.9–1.6)	0.17
2016	0.9 (0.7–1.2)	0.53	1 (0.7–1.3)	0.73
2017	1 (0.8–1.3)	0.84	1.2 (0.9–1.5)	0.34
Epilepsy type				
Focal	1.7 (1.4–2)	<0.01	1.3 (1.1–1.6)	<0.01
Generalized	Reference		Reference	
Unknown	1.2 (1–1.4)	0.05	1.2 (1–1.5)	0.05
Disease severity (in prior 2 years)				
3+ ASMs	1.5 (1.4–1.8)	<0.01	1.6 (1.3–1.8)	<0.01
Prior hospitalizations	1.6 (1.4–1.9)	<0.01	1.7 (1.4–2)	<0.01
Prior ED visit	1.5 (1.3–1.7)	<0.01	1.4 (1.2–1.6)	<0.01
Neurologic comorbidities				
TBI	1.4 (1.1–1.8)	0.02	1.3 (0.9–1.8)	0.11
Headache	1.3 (1.1–1.5)	<0.01	1.4 (1.1–1.6)	<0.01
Stroke	1.1 (1–1.3)	0.08	1.1 (0.9–1.3)	0.47
Dementia	0.9 (0.7–1)	0.1	0.8 (0.7–1)	0.08
Brain tumor	1.2 (0.9–1.6)	0.14	1.4 (1.04–1.9)	0.03
Intellectual disability/ developmental delay	1.1 (0.9–1.3)	0.29	1 (0.8–1.2)	0.86
Psychiatric comorbidities				
Anxiety	1.1 (1–1.3)	0.12	1.1 (1–1.3)	0.16

TABLE 3 (Continued)

	Full cohort model: Patients of all providers		Subanalysis model: Patients of neurologists	
	LTM or surgery multivariable OR (95% CI) $N = 11\,907$ *c* statistic = 0.93	*p* value	LTM or surgery multivariable OR (95% CI) $N = 7913$ *c* statistic = 0.88	*p* value
Depression	1.1 (0.9–1. 2)	0.6	1.1 (0.9–1.3)	0.56
Bipolar disorder	0.8 (0.7–1)	0.08	0.9 (0.7–1.1)	0.18
Alcohol/substance abuse	1.1 (0.9–1.3)	0.43	1 (0.8–1.2)	0.91
PNES	1.6 (1.1–2.3)	0.03	1.6 (1–2.7)	0.05
Charlson score (excluding dementia, stroke)				
0	Reference		Reference	
1	1.1 (0.9–1.3)	0.29	1.1 (0.9–1.3)	0.34
2	1 (0.8–1.2)	0.69	1 (0.9–1.3)	0.69
3+	1 (0.8–1.1)	0.75	1 (0.8–1.2)	0.91
Diagnosing physician				
Neurologist	1.9 (1.6–2.3)	<0.01	–	–
Neurosurgeon	7 (4.1–11.8)	<0.01	–	–
EM	1.7 (1.3–2.3)	<0.01	–	–
PCP	Reference		–	–
NP or PA	1.4 (1.01–2.1)	0.04	–	–
Other	2 (1.5–2.7)	<0.01	–	–
Neurologist density quintile				
1st quintile (low)	Reference		Reference	
2nd quintile	1 (0.8–1.3)	0.82	0.8 (0.6–1.1)	0.23
3rd quintile	0.8 (0.7–1.1)	0.18	0.9 (0.7–1.2)	0.39
4th quintile	1 (0.8–1.3)	0.87	0.9 (0.7–1.2)	0.35
5th quintile (high)	1.5 (1.2–1.9)	<0.01	1.2 (0.9–1.6)	0.19
Prior LTM EEG	1.8 (1.5–2.2)	<0.01	1.5 (1.2–1.9)	<0.01
Distance to nearest epilepsy center				
<50 miles	1.5 (1.3–1.7)	<0.01	1.2 (1–1.4)	0.09
50+ miles	Reference		Reference	
Provider sex				
Female	–	–	1 (0.8–1.1)	0.61
Provider graduation date <10 years	–	–	1.5 (1.2–1.8)	<0.01
Provider census region				
Northeast	–	–	Reference	
Midwest	–	–	0.7 (0.5–0.9)	<0.01
South	–	–	0.8 (0.6–0.95)	0.02
West	–	–	0.7 (0.5–0.9)	<0.01
Outside of US/unknown	–	–	1.5 (0.1–28.1)	0.78
Epilepsy specialist provider	–	–	2.5 (2.1–3)	<0.01
Provider in epilepsy center ZIP	–	–	2 (1.7–2.3)	<0.01

PNES diagnosis, prior hospitalization, and proximity to an epilepsy center. Being diagnosed by a non-PCP provider (neurologist, neurosurgeon, or emergency medicine physician) and factors associated with better access to care (residing in a higher neurologist density region, prior LTM completion) as well as certain provider characteristics

(more recently graduated, epilepsy-specialized) were also associated with LTM. Our models performed very well at discriminating which patients would complete LTM. Most importantly, we found that the provider-to-provider variation, even between neurologists, explained a large amount of variation in whether a patient completed LTM.

Most patients diagnosed with drug-resistant epilepsy (77%) never underwent LTM. This is concerning as referral to an epilepsy center for evaluation has been proposed since the 2003 AAN practice parameter[31] and was reiterated in the current 2017 AAN Epilepsy Quality Measurement set.[32] Nonetheless, our findings are in keeping with previously published estimates of referral to a comprehensive epilepsy center, best practically measured by LTM completion since referral itself does not generate a claim. One study of adults with drug-resistant epilepsy in Ontario, Canada found only 2.2% underwent prolonged video EEG monitoring within 2 years of diagnosis.[13] Another study of people <65 years of age with persistent seizures in California found 3.9% underwent video EEG monitoring.[14] Our finding that 19% of patients underwent LTM after drug-resistant epilepsy diagnosis is greater than these prior studies likely due to a broader definition of LTM and longer follow-up period. Our chosen definition was intended to bias away from undercounting and yet the magnitude of non-referral remains impressive. In our study, only 2.4% of patients with drug-resistant epilepsy underwent therapeutic epilepsy surgery of any type. This estimate was in keeping with the above-mentioned study of a Canadian population (1.2% underwent surgery).[13]

Our results further support that epilepsy surgery is underutilized, even when including both neurostimulation and resective surgeries as well as lengthening follow-up time. If all patients with drug-resistant epilepsy underwent surgical evaluation it is likely more surgical candidates would be identified, although those currently undergoing surgical evaluation may be those most amenable to surgery and therefore surgical rates may not increase proportionately. A specific challenge in increasing surgical referral is the infrequent presentation of drug-resistant epilepsy: an average 2% of neurologists' practice and 11% of epilepsy specialists' practice. One tool that could promote assessment of infrequent presentations is the online tool developed by Jette et al. to assess whether a patient should be referred for epilepsy surgery evaluation.[33]

Our data suggest greater distance from an epilepsy center may be a barrier to referral for LTM. A recent analysis of epilepsy center locations noted that epilepsy centers tend to cluster in populous cities and are less prevalent in regions with lower area deprivation indices.[34] Thus opportunities for virtual epilepsy care, such as televisits and e-consults, may be particularly important to improving disparities. Inpatient LTM cannot be completed remotely, but preliminary telemedicine consultation might encourage a patient to travel for evaluation and many initial data considered (e.g., EEG, brain MRI, ASM history, seizure semiology, and frequency) are well-suited to remote review. Studies of virtual epilepsy care have demonstrated patient satisfaction[35] and positive provider views.[36] As a strategy paired with the expansion of telemedicine for presurgical evaluation, financial support/reimbursement for patient travel (such as non-emergency medical transport [NEMT] to medical appointments of Medicaid beneficiaries) for LTM admissions may be advantageous policy.

Our models strongly predicted referral to LTM (model of all providers: c statistic 0.94; model of neurologist providers: c statistic 0.89). We found several patient factors associated with LTM referral, yet we identified no dominant patient predictors (aOR ranging from 1.2 to 1.7). This may be expected due to the complexity of patient presentations, breadth of relevant considerations in presurgical evaluation initiation, and poor capture of clinical decision-making in administrative claims data. Prior studies have demonstrated similar predictors for LTM or epilepsy surgery completion (younger age and female sex as well as additional predictors of white race and fewer comorbidities)[13,14]; these prior studies similarly were unable to identify one or two dominant predictors. Notably, we did find provider factors had slightly greater effect (aOR 1.5–2.6), which is encouraging as these are factors that are likely more amenable to intervention.

While it is intuitive that individual provider practice and environment could impact referral, we have not previously seen explicit measure of this. Our results demonstrate provider-to-provider variation explained a sizable proportion of the variation in who received LTM (42% in the all-provider model and 37% in the neurologist model). These findings should focus future efforts to achieve improved referral. Prior investigations have described inadequate neurologist knowledge as a key barrier,[16,37] which might encourage educational interventions and our data do show more recent graduates are more likely to refer. However, it is not clear that knowledge base is the *greatest* issue, particularly as demonstrated by lower-than-expected referral by providers within a tertiary epilepsy center clinic.[15] Furthermore, educational countermeasures may improve knowledge without achieving sustainability or change in clinical practice. If certain environments tend to be referral-friendly or referral-unfriendly, a better understanding of the context in which providers practice could improve the uptake. Prior provider surveys have found important reasons for non-referral to include concerns about surgery risk, insufficient resources, variable attitude toward

epilepsy surgery, and dissatisfaction with communication with epilepsy centers.[17,18,38] A deeper and broader characterization of provider-level concerns and the hierarchy of these concerns is warranted.

5 | LIMITATIONS

This paper presumes all patients with drug-resistant epilepsy warrant LTM; there may be some for whom LTM is not indicated. While epilepsy severity may not be perfectly captured by administrative claims data,[21] we did measure many factors that could influence surgical decision-making (epilepsy type, ASM number, hospitalizations/ED visits for seizures, etc.). It can be difficult to define incident diagnoses and we would miss relevant healthcare use prior to Medicare enrollment; however, we used a minimum standard washout period of 2 years[39,40] and were able to query claims through 2001 which made long-standing diagnoses of drug-resistant epilepsy less likely. In this study, we cannot quantify patients for whom LTM referral was recommended but the patient declined or LTM was never scheduled; patient-related factors are important to this research question but were not measurable with our dataset and were outside the scope of this analysis. Lastly, we chose to use Medicare data for this analysis because Medicare insures a large proportion of patients with drug-resistant epilepsy,[9] given a substantial number of patients with active epilepsy are disabled.[23] Additionally Medicare data was critical for including geographic implications and provider characteristics. It will be important to perform similar analyses on alternative datasets to better understand referral for patients with employer-based insurance, as some prior studies have suggested Medicare beneficiaries may be less likely to undergo epilepsy surgery compared to those privately insured.[9,14,41]

6 | CONCLUSIONS

We found that a small proportion (19%) of Medicare beneficiaries with drug-resistant epilepsy initiated the presurgical evaluation pathway. Several patient characteristics, non-PCP diagnosing physician, and measures of access to care were the strongest predictors. We found that a large proportion of variation in referral was explained by provider or environmental factors, even among patients of neurologists. Thus, epilepsy systems of care may provide a target for further research and future interventions to improve referral of patients for evaluation for epilepsy surgery candidacy.

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CONFLICT OF INTEREST STATEMENT

None of the authors have any relevant conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

This study was performed using Medicare data, which is publicly available.

ETHICS STATEMENT

The University of Michigan Institutional Review Board determined that this study was exempt. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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